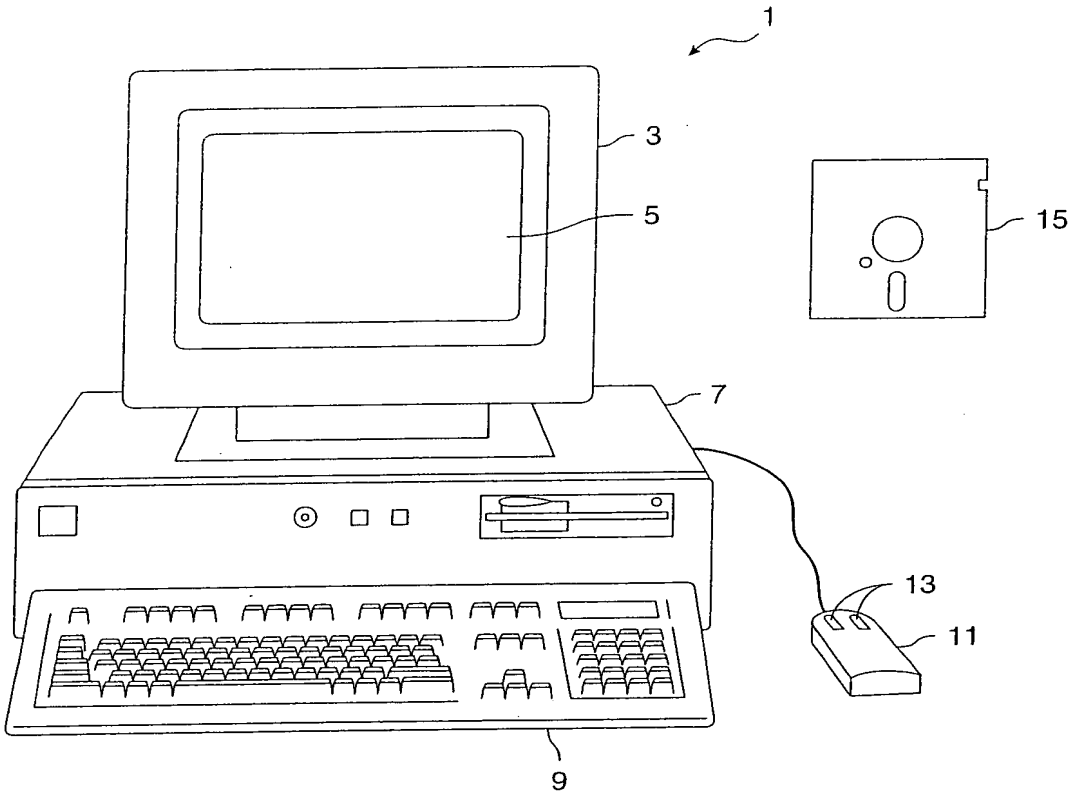

1
3
5
15
7
13
11
9

FIG. 1

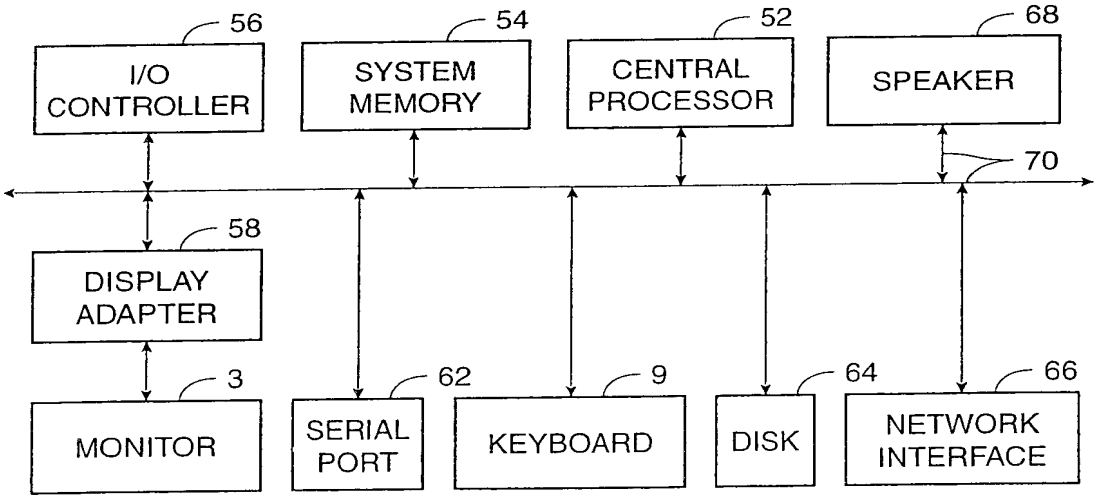

56
I/O CONTROLLER
54
SYSTEM MEMORY
52
CENTRAL PROCESSOR
68
SPEAKER
70
58
DISPLAY ADAPTER
3
MONITOR
62
SERIAL PORT
9
KEYBOARD
64
DISK
66
NETWORK INTERFACE

FIG. 2

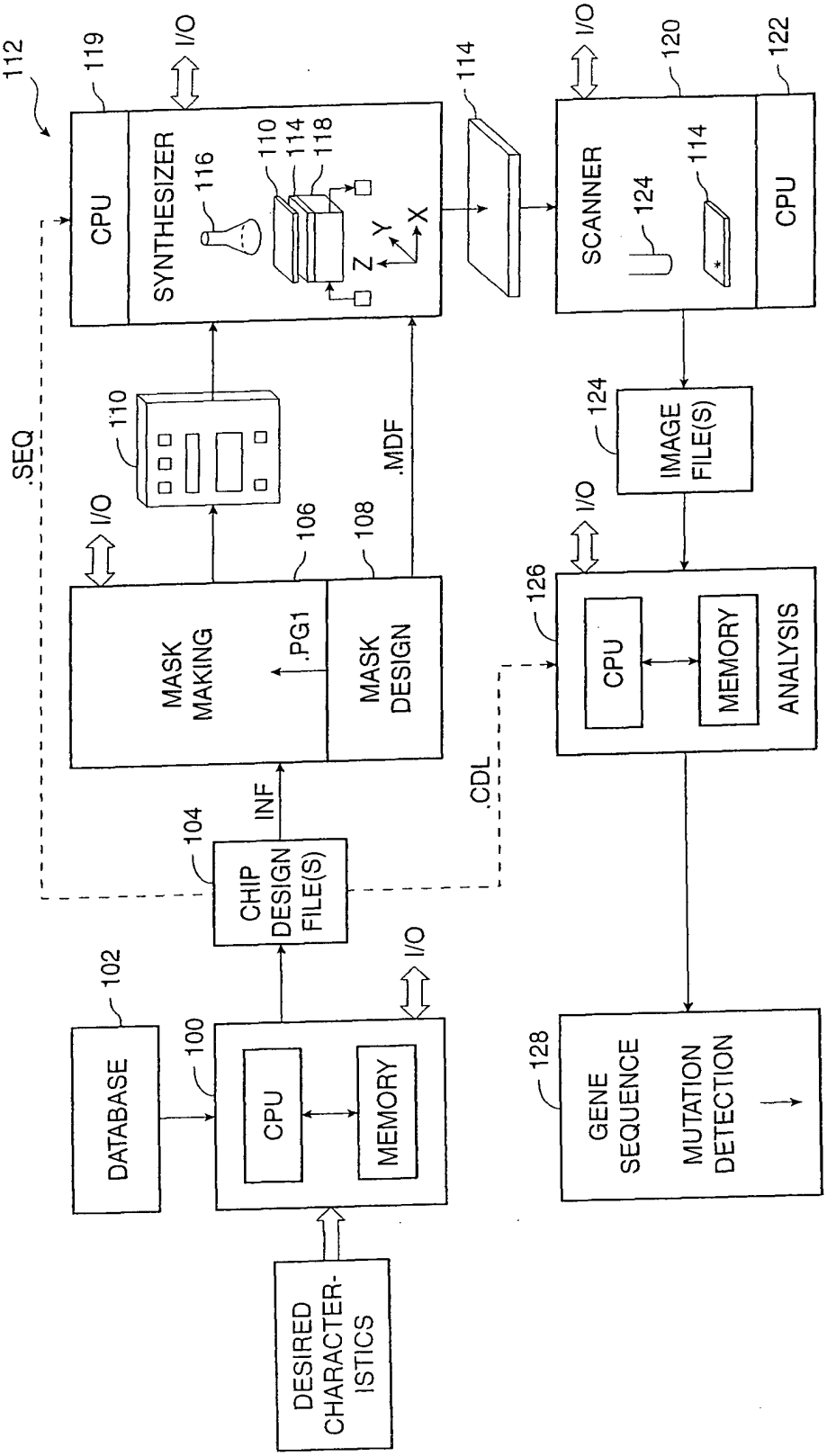

DESIRED CHARACTER-ISTICS
DATABASE
102
100
CPU
MEMORY
I/O
CHIP DESIGN FILE(S)
104
INF
.CDL
.SEQ
MASK MAKING
.PG1
MASK DESIGN
106
108
I/O
110
.MDF
112
CPU
SYNTHESIZER
116
110
114
118
Z
Y
X
119
I/O
114
SCANNER
124
114
CPU
120
122
I/O
IMAGE FILE(S)
124
126
CPU
MEMORY
ANALYSIS
GENE SEQUENCE
MUTATION DETECTION
128

FIG. 3

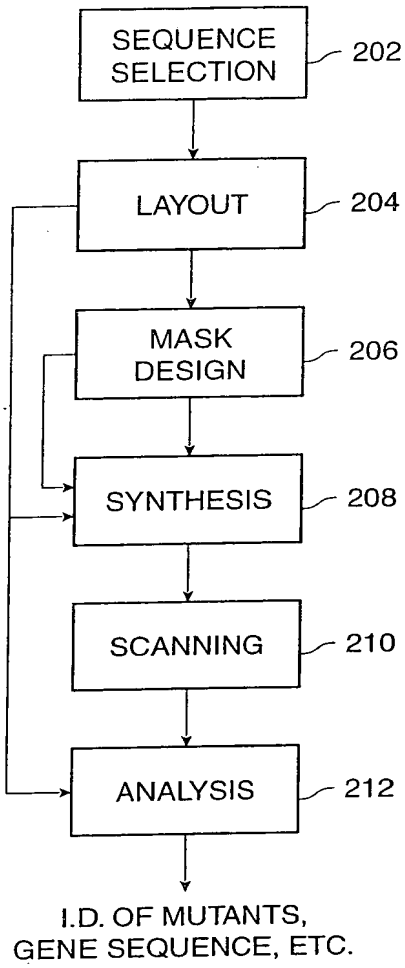

SEQUENCE SELECTION
202
LAYOUT
204
MASK DESIGN
206
SYNTHESIS
208
SCANNING
210
ANALYSIS
212
I.D. OF MUTANTS, GENE SEQUENCE, ETC.

FIG. 4

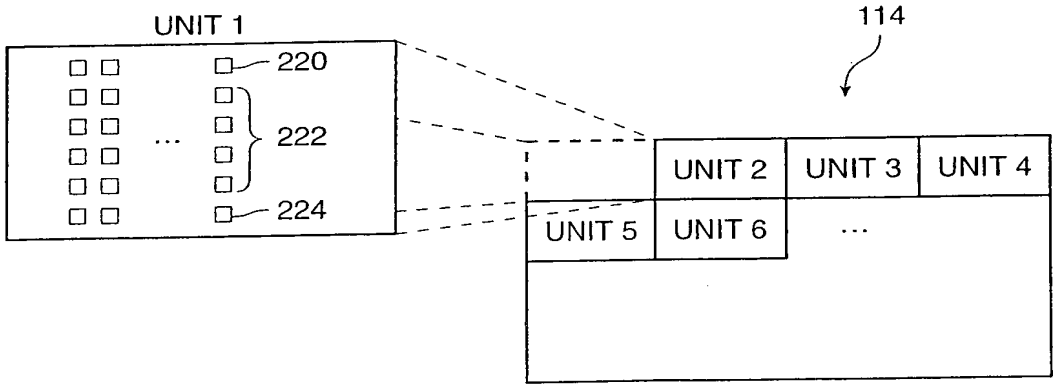

UNIT 1
220
222
224
114
UNIT 2
UNIT 3
UNIT 4
UNIT 5
UNIT 6

FIG. 5

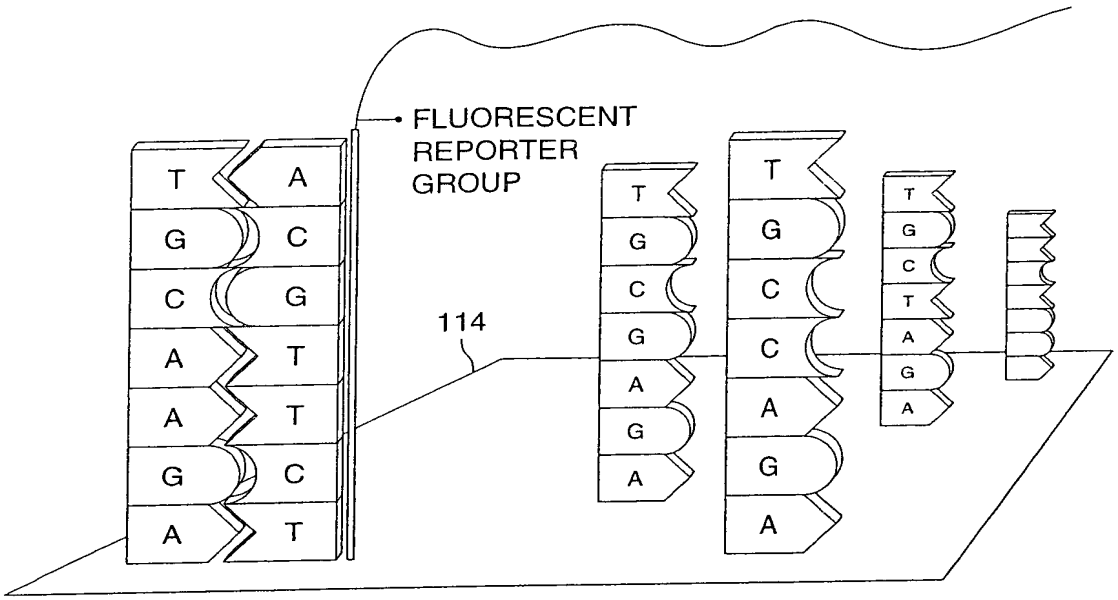


FIG. 6

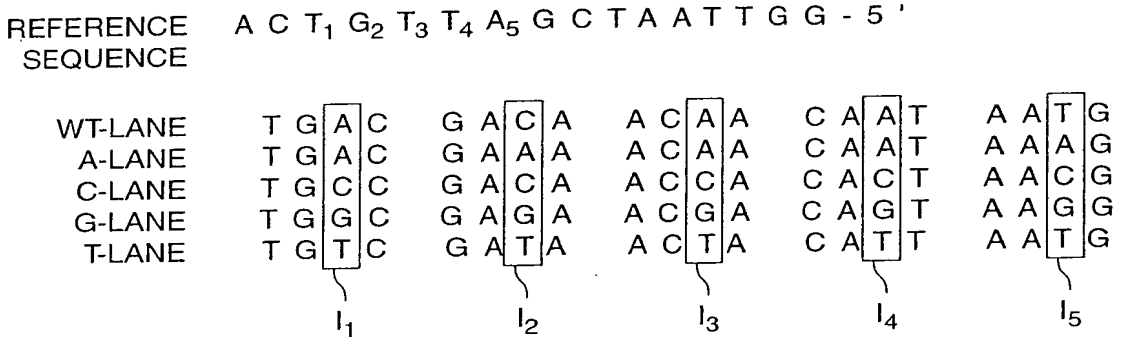


FIG. 7

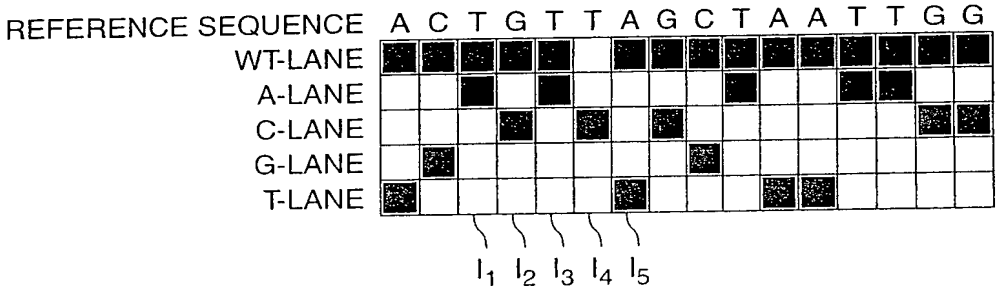


FIG. 8

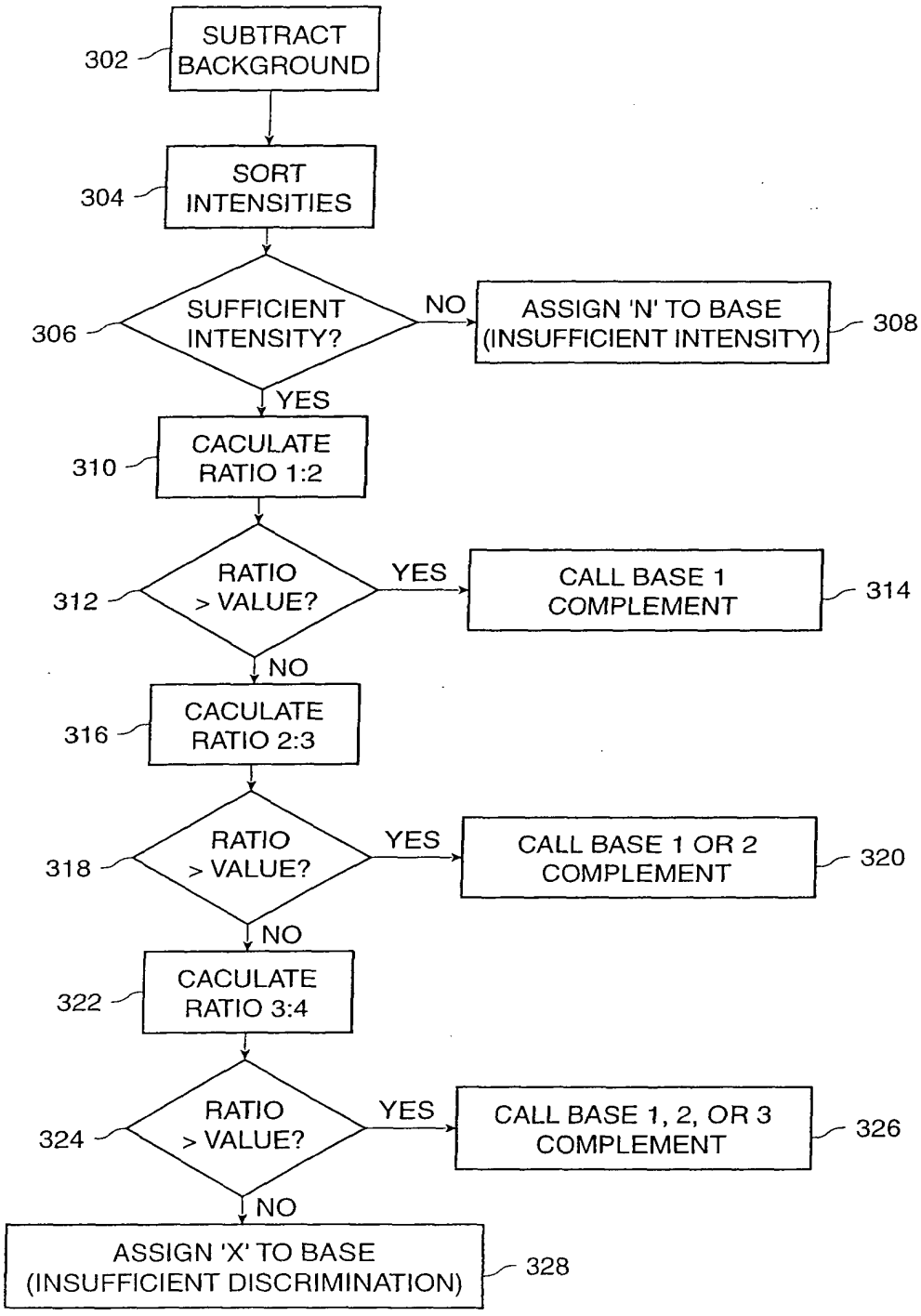

302
SUBTRACT BACKGROUND
304
SORT INTENSITIES
306
SUFFICIENT INTENSITY?
NO
ASSIGN 'N' TO BASE (INSUFFICIENT INTENSITY)
308
YES
310
CACULATE RATIO 1:2
312
RATIO > VALUE?
YES
CALL BASE 1 COMPLEMENT
314
NO
316
CACULATE RATIO 2:3
318
RATIO > VALUE?
YES
CALL BASE 1 OR 2 COMPLEMENT
320
NO
322
CACULATE RATIO 3:4
324
RATIO > VALUE?
YES
CALL BASE 1, 2, OR 3 COMPLEMENT
326
NO
ASSIGN 'X' TO BASE (INSUFFICIENT DISCRIMINATION)
328

FIG. 9

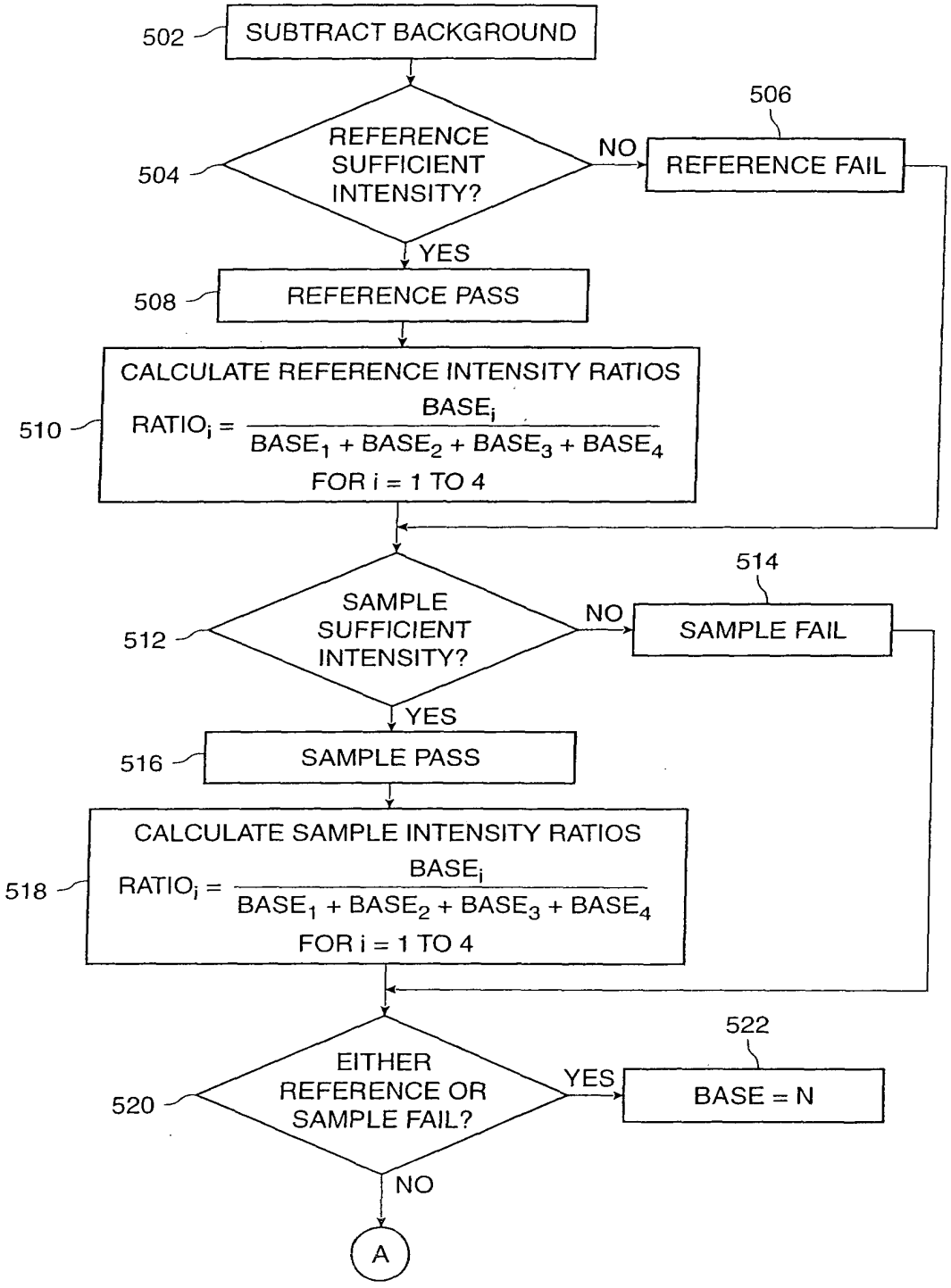

502
SUBTRACT BACKGROUND
504
REFERENCE SUFFICIENT INTENSITY?
NO
506
REFERENCE FAIL
YES
508
REFERENCE PASS
510
CALCULATE REFERENCE INTENSITY RATIOS
$RATIO_i = \frac{BASE_i}{BASE_1 + BASE_2 + BASE_3 + BASE_4}$
FOR i = 1 TO 4
512
SAMPLE SUFFICIENT INTENSITY?
NO
514
SAMPLE FAIL
YES
516
SAMPLE PASS
518
CALCULATE SAMPLE INTENSITY RATIOS
$RATIO_i = \frac{BASE_i}{BASE_1 + BASE_2 + BASE_3 + BASE_4}$
FOR i = 1 TO 4
520
EITHER REFERENCE OR SAMPLE FAIL?
YES
522
BASE = N
NO
A

FIG. 10A

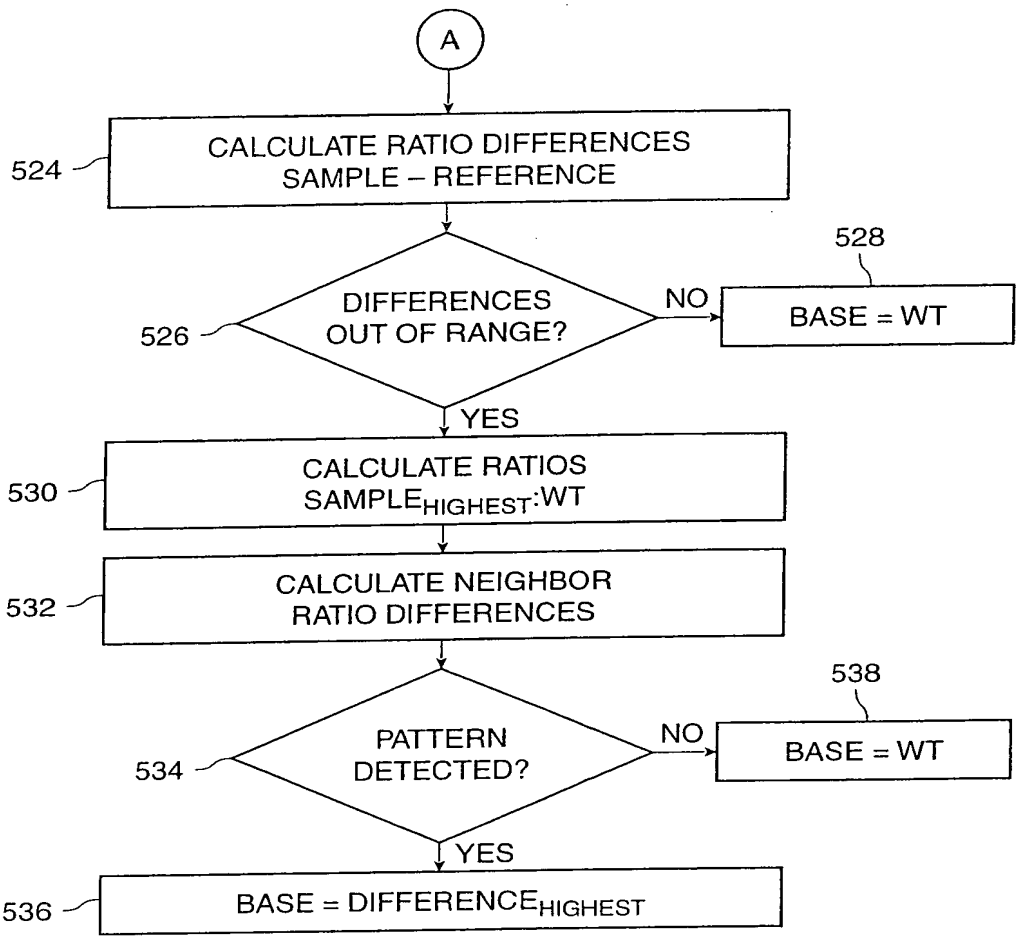


FIG. 10A
(CONTINUED)

		REFERENCE					SAMPLE					RATIO OF RATIOS					
POSITION	WT	BACK-GROUND	A	C	G	T	BACK-GROUND	A	C	G	T	A/A	C/C	G/G	T/T	BASE	CONFIDENCE
463	C	P	7.2	9.9	1.0	5.6	P	6.4	2.3	1.0	14.5	1.1	4.3	1.0	0.4	G	1
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18

FIG. 10B

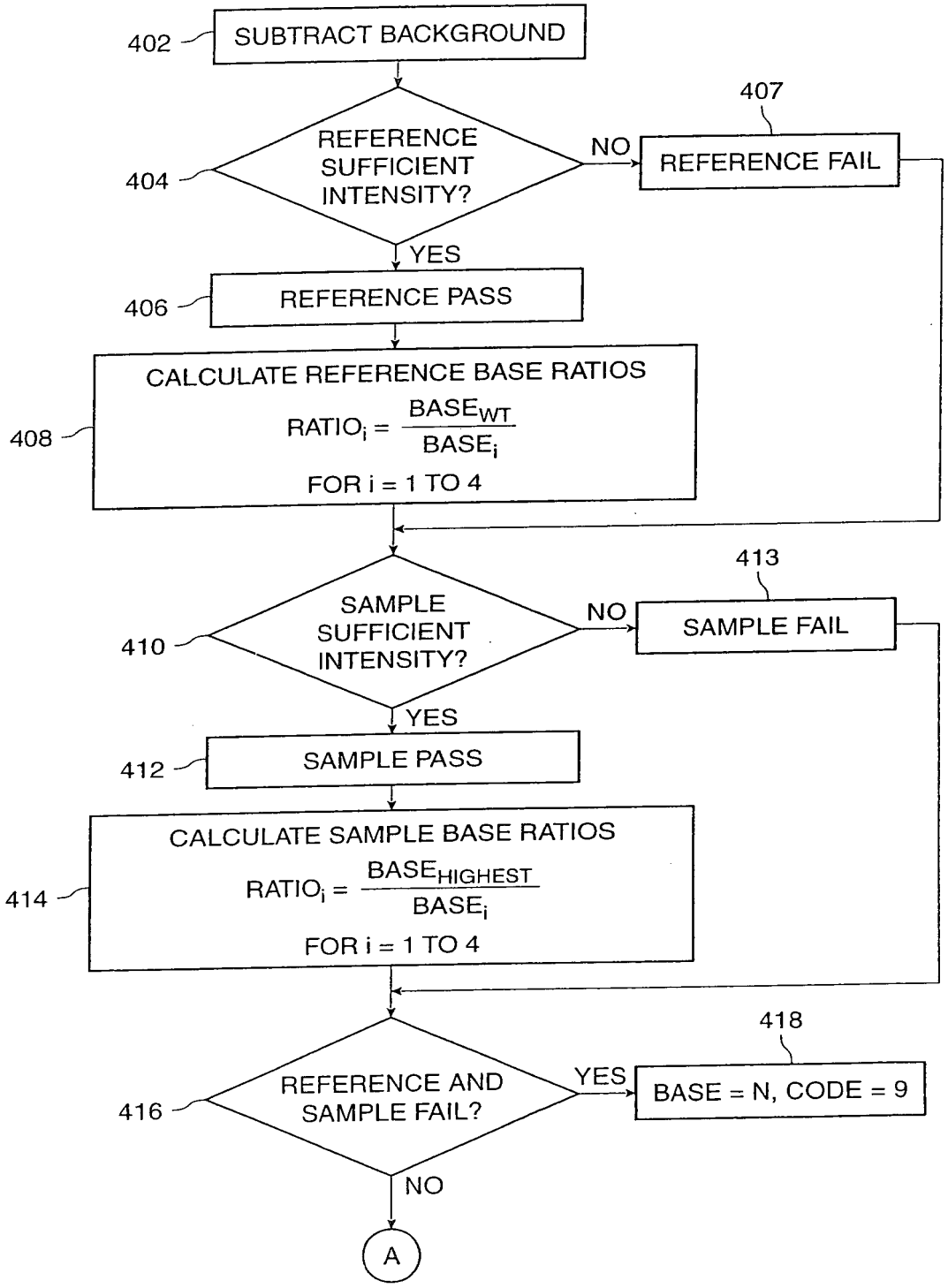

402
SUBTRACT BACKGROUND
404
REFERENCE SUFFICIENT INTENSITY?
NO
407
REFERENCE FAIL
YES
406
REFERENCE PASS
408
CALCULATE REFERENCE BASE RATIOS
$RATIO_i = \frac{BASE_{WT}}{BASE_i}$
FOR i = 1 TO 4
410
SAMPLE SUFFICIENT INTENSITY?
NO
413
SAMPLE FAIL
YES
412
SAMPLE PASS
414
CALCULATE SAMPLE BASE RATIOS
$RATIO_i = \frac{BASE_{HIGHEST}}{BASE_i}$
FOR i = 1 TO 4
416
REFERENCE AND SAMPLE FAIL?
YES
418
BASE = N, CODE = 9
NO
A

FIG. 11A

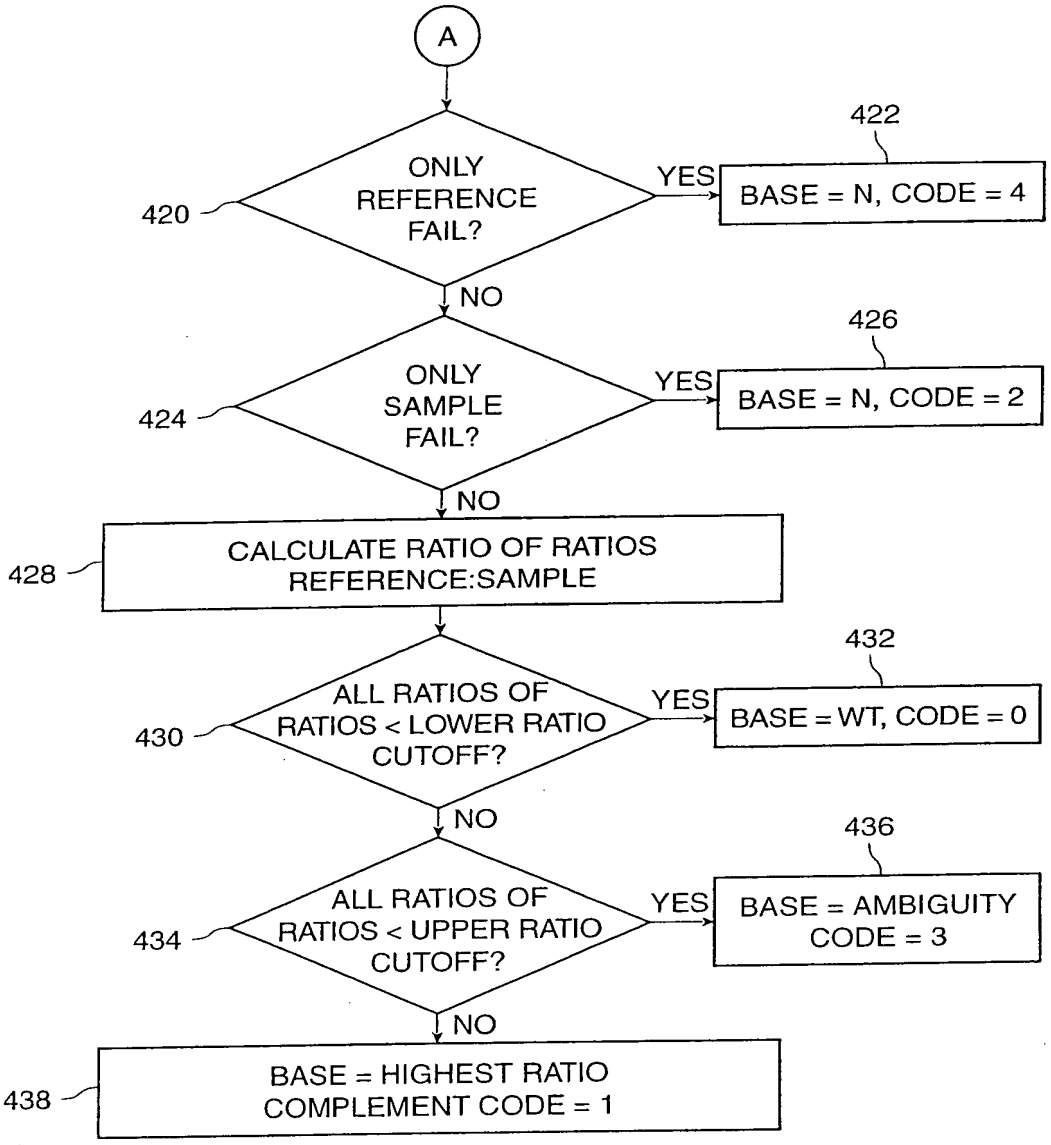


FIG. 11A
(CONTINUED)

BCK SUBTRACTED INTENSITIES																	
RY090203.CQ1	-7	-6	-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9
POSITION:	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250
WILDTYPE:	A	A	A	C	C	C	A	A	T	C	C	A	C	A	T	C	A
CALLED:	A	A	A	C	C	C	A	A	T	C	C	A	C	A	T	C	M
A	148	193	165	17	70	38	282	385	97	31	18	158	15	223	178	126	154
C	57	100	42	167	345	278	38	99	139	249	249	13	244	28	257	250	175
G	26	32	20	16	64	17	27	107	100	13	9	11	10	30	142	59	55
T	9	15	10	6	41	14	27	79	261	6	2	1	7	16	320	52	37
S	240	340	238	207	522	347	374	671	598	298	279	182	276	298	896	487	421
WTR	148	193	165	167	345	278	282	385	261	249	249	158	244	223	320	250	154
MAXR	148	193	165	167	345	278	282	385	261	249	249	158	244	223	320	250	175
MC090407.CQ1																	
POSITION:																	
WILDTYPE:	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250
CALLED:	A	A	A	C	C	C	A	A	T	C	C	A	C	A	T	C	A
A	M	M	A	C	X	C	A	X	X	C	C	A	C	A	X	X	M
C	194	238	150	44	191	126	283	332	234	58	49	242	25	337	286	180	256
G	209	291	74	202	337	277	74	199	175	259	288	27	376	65	379	324	234
T	92	72	34	29	114	52	65	571	231	30	17	16	47	71	254	104	109
S	25	39	16	11	96	29	68	205	267	11	8	5	23	57	427	97	85
WTR	520	639	274	286	738	484	489	1307	906	357	362	291	472	529	1346	705	684
MAXR	194	238	150	202	337	277	283	332	267	259	288	242	376	337	427	324	256
	209	291	150	202	337	277	283	571	267	259	288	242	376	337	427	324	256

502A

502B

FIG. 11B

WTE/WTR	1.31	1.23	0.91	1.21	0.98	1.00	1.00	0.86	1.02	1.04	1.15	1.54	1.54	1.51	1.34	1.30	1.66
MAXE/WTR	1.42	1.51	0.91	1.21	0.98	1.00	1.00	1.48	1.02	1.04	1.15	1.54	1.54	1.51	1.34	1.30	1.66
N-L + N-R		0.79	-0.63	0.54	-0.25	0.01	0.14	0.94	0.14	-0.10	-0.27	0.38	0.04	0.14	-0.13	-0.40	
N-L		0.09	-0.60	0.30	-0.24	0.02	0.01	0.48	-0.46	0.02	0.11	0.38	0.01	-0.04	-0.17	-0.04	
N-R		0.60	-0.30	0.24	-0.02	-0.01	-0.48	0.46	-0.02	-0.11	-0.38	-0.01	0.04	0.17	0.04	-0.36	
N-L D(N-R)			-0.90	0.54	-0.25	0.01	-0.48	0.94	-0.48	-0.10	-0.27	0.38	0.04	0.14	-0.13		
N-R D(N-L)			-0.90	0.54	-0.25	0.01	-0.48	0.94	-0.48	-0.10	-0.27	0.38	0.04	0.14	-0.13		
L(N-L) - (N-R)L			0.29	0.07	0.22	0.02	0.49	0.02	0.44	0.13	0.50	0.39	0.03	0.21	0.21		
A+B-C			-2.10	1.01	-0.73	0.00	-1.44	1.86	-1.40	-0.33	-1.03	0.36	0.06	0.06	-0.48		
SUM MT/ SUM WT																	
INTENSITIES																	
N/L + N/R	2.16	1.88	1.15	1.39	1.41	1.39	1.31	1.95	1.52	1.20	1.30	1.60	1.71	1.78	1.50	1.45	1.63
N-L + N-R		2.50	1.45	2.18	2.04	2.05	1.61	2.77	2.04	1.71	1.89	2.18	2.03	2.22	1.88	1.85	
N-L		0.22	-0.48	0.10	0.02	0.03	-0.36	0.54	-0.06	-0.21	-0.10	0.10	0.02	0.17	-0.11	-0.12	
N-R		-0.28	-0.73	0.21	0.03	-0.02	-0.09	0.54	-0.43	-0.32	0.10	0.30	0.10	0.07	-0.27	-0.06	
		0.73	-0.23	-0.03	0.02	0.09	-0.64	0.43	0.32	-0.10	-0.30	-0.10	-0.07	0.27	0.06	-0.18	

530

532

FIG. 11B
(CONTINUED)

NORMALIZED INTENSITIES																	
WILDTYPE																	
A	0.61	0.57	0.70	0.08	0.13	0.11	0.75	0.57	0.16	0.10	0.07	0.87	0.06	0.75	0.20	0.26	0.37
C	0.24	0.29	0.18	0.81	0.66	0.80	0.10	0.15	0.23	0.83	0.90	0.07	0.88	0.09	0.29	0.51	0.42
G	0.11	0.09	0.08	0.08	0.12	0.05	0.07	0.16	0.17	0.04	0.03	0.06	0.04	0.10	0.16	0.12	0.13
T	0.04	0.04	0.04	0.03	0.08	0.04	0.07	0.12	0.44	0.02	0.01	0.01	0.03	0.05	0.36	0.11	0.09
MUTANT																	
A																	
C	0.37	0.37	0.55	0.15	0.26	0.26	0.58	0.25	0.26	0.16	0.16	0.83	0.05	0.64	0.21	0.26	0.37
G	0.40	0.45	0.27	0.71	0.46	0.57	0.15	0.15	0.19	0.72	0.80	0.09	0.80	0.12	0.28	0.46	0.34
T	0.18	0.11	0.12	0.10	0.15	0.11	0.13	0.44	0.25	0.08	0.05	0.06	0.10	0.13	0.19	0.15	0.16
MT - MT (NORMALIZED	0.05	0.06	0.06	0.04	0.13	0.06	0.14	0.16	0.29	0.03	0.02	0.02	0.05	0.11	0.32	0.14	0.12
INTENSITIES)																	
POSITION:																	
WILDTYPE:																	
CALLED:	234	235	236	237	238	239	240	241	242	243	244	245	246	247	248	249	250
A	A	A	A	C	C	C	A	A	T	C	C	A	C	A	T	C	A
C	M	M	A	C	X	C	A	X	X	C	C	A	C	A	X	X	M
G	-0.24	-0.20	-0.15	0.07	0.12	0.15	-0.18	-0.32	0.09	0.06	0.07	-0.04	0.00	-0.11	0.01	0.00	0.01
T	0.17	0.16	0.09	-0.10	-0.20	-0.23	0.05	0.00	-0.04	-0.11	-0.10	0.03	-0.08	0.03	-0.01	-0.05	-0.07
	0.07	0.02	0.04	0.02	0.03	0.06	0.06	0.28	0.09	0.04	0.01	0.00	0.06	0.03	0.03	0.03	0.03
	0.01	0.02	0.02	0.01	0.05	0.02	0.07	0.04	-0.14	0.01	0.01	0.01	0.02	0.05	-0.04	0.03	0.04

510

518

524

FIG. 11B
(CONTINUED)

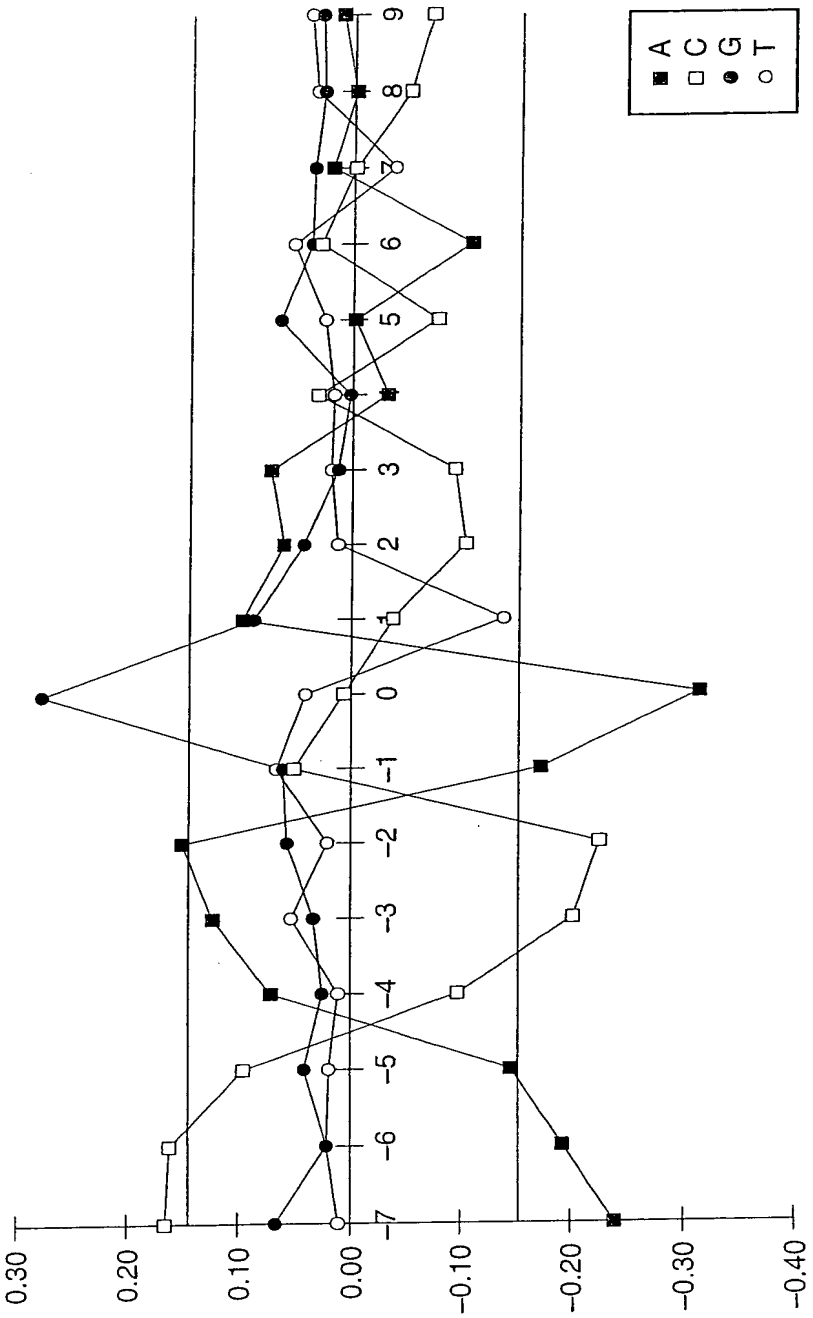


FIG. 11C

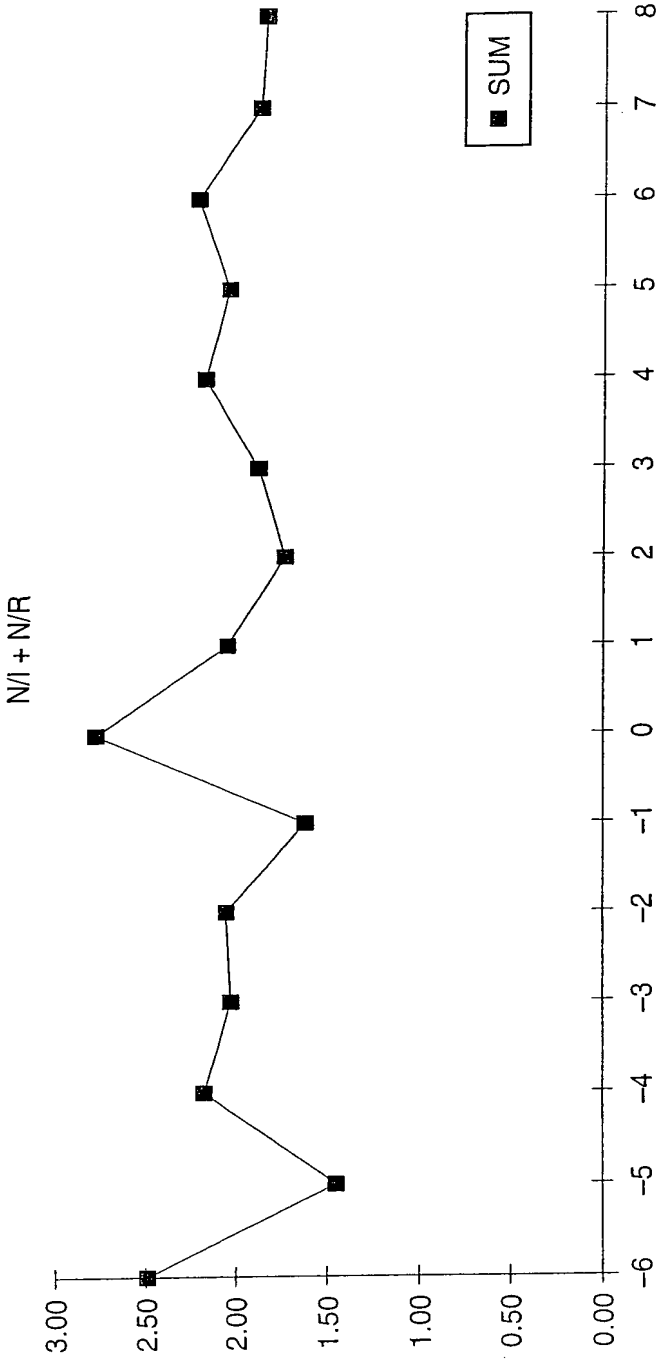


FIG. 11D

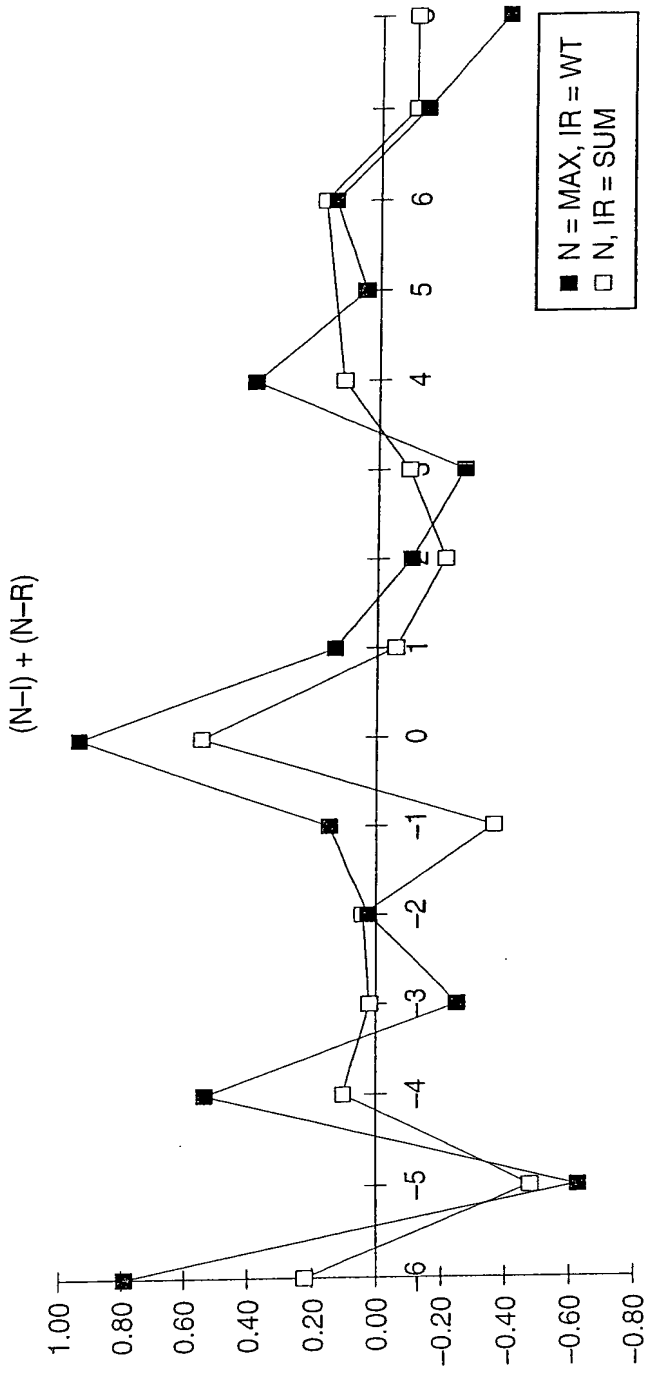


FIG. 11D (CONTINUED)

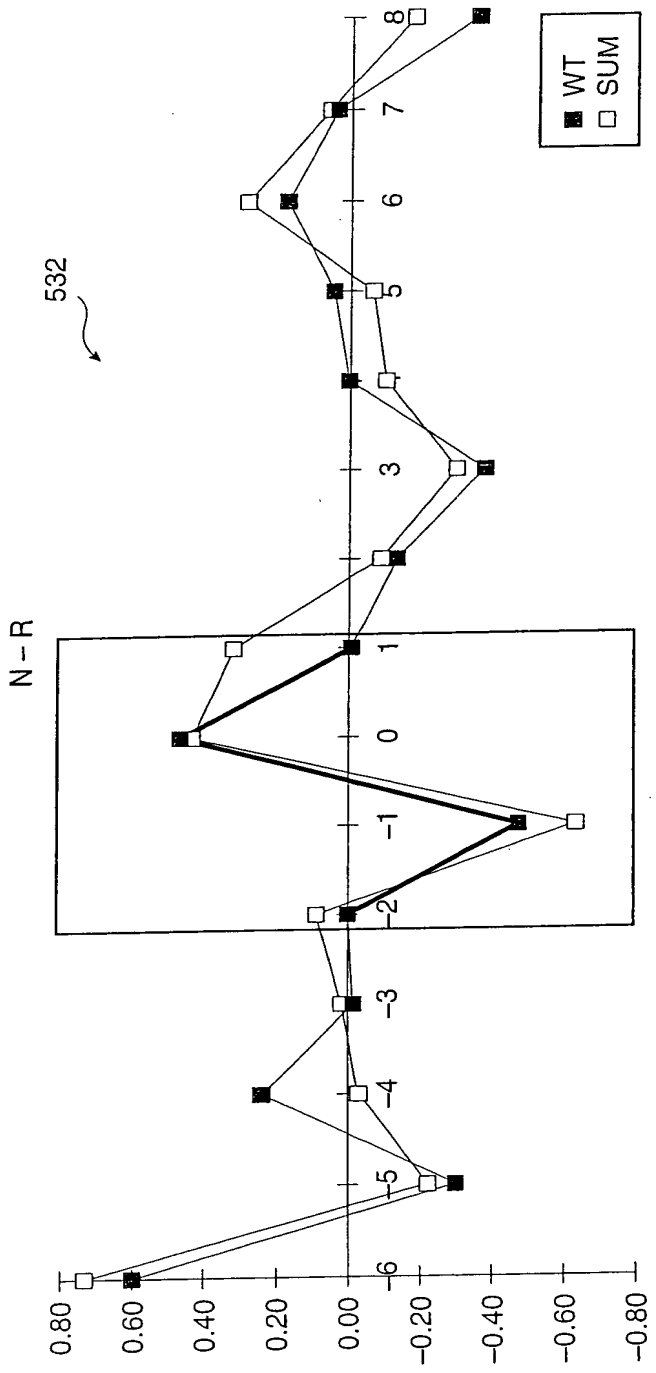


FIG. 11D
(CONTINUED)

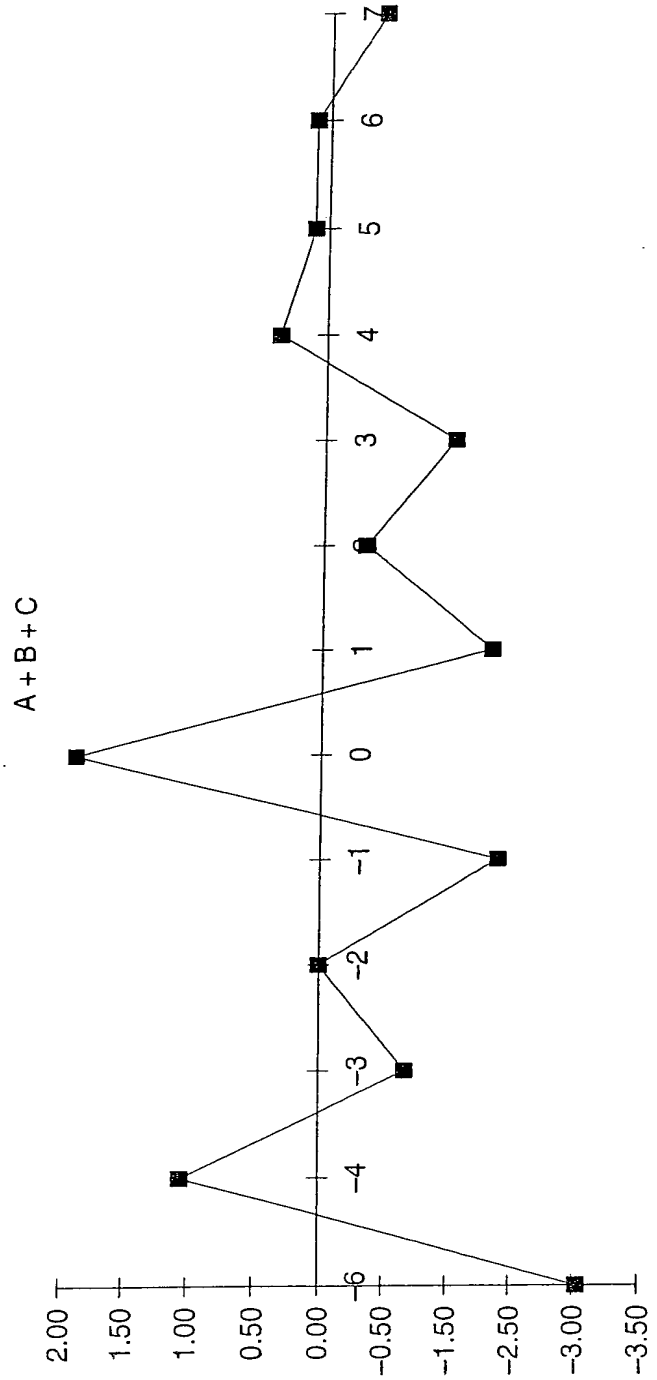


FIG. 11D
(CONTINUED)

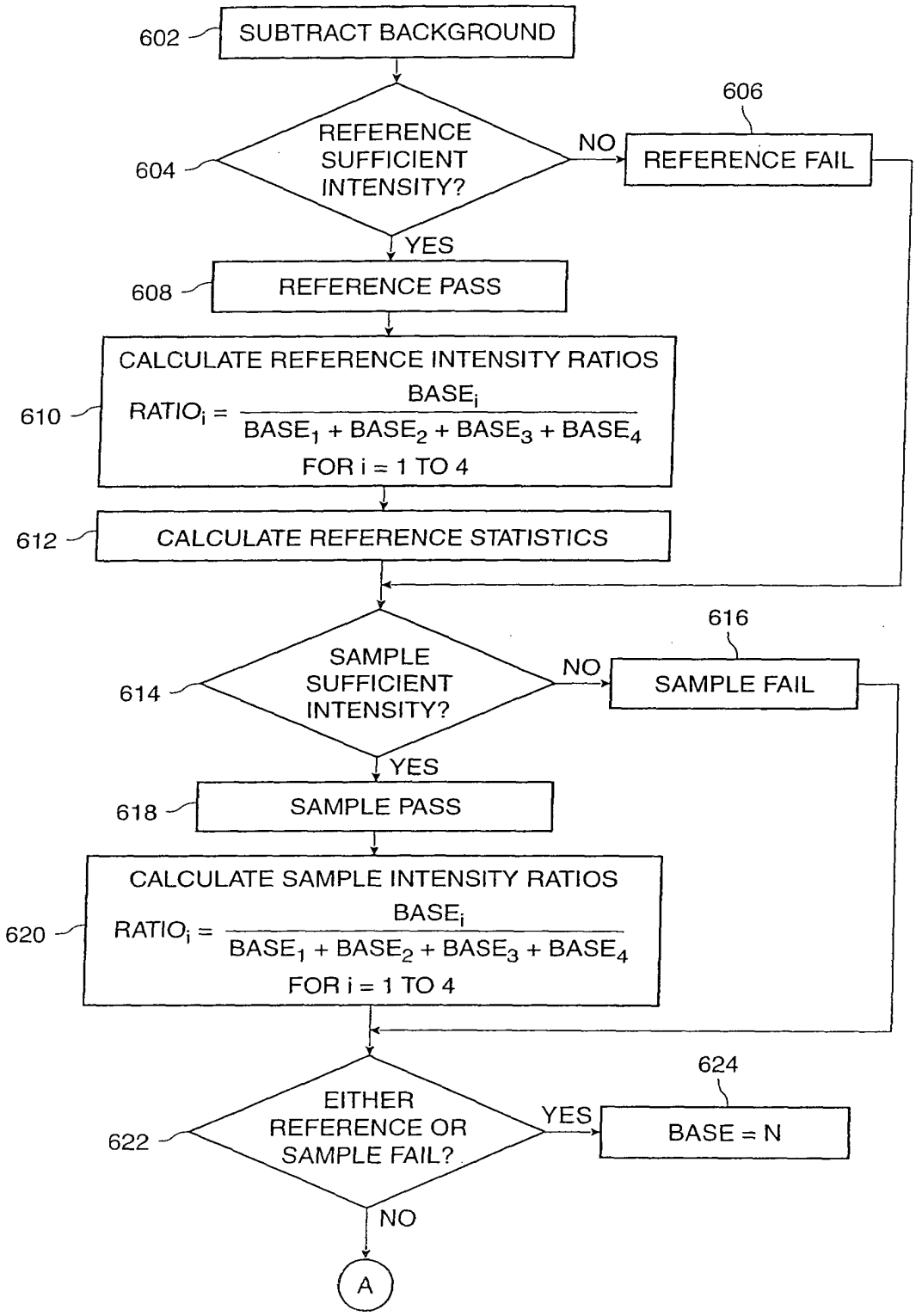

602
SUBTRACT BACKGROUND
604
REFERENCE SUFFICIENT INTENSITY?
NO
606
REFERENCE FAIL
YES
608
REFERENCE PASS
610
CALCULATE REFERENCE INTENSITY RATIOS
$RATIO_i = \frac{BASE_i}{BASE_1 + BASE_2 + BASE_3 + BASE_4}$
FOR i = 1 TO 4
612
CALCULATE REFERENCE STATISTICS
614
SAMPLE SUFFICIENT INTENSITY?
NO
616
SAMPLE FAIL
YES
618
SAMPLE PASS
620
CALCULATE SAMPLE INTENSITY RATIOS
$RATIO_i = \frac{BASE_i}{BASE_1 + BASE_2 + BASE_3 + BASE_4}$
FOR i = 1 TO 4
622
EITHER REFERENCE OR SAMPLE FAIL?
YES
624
BASE = N
NO
A

FIG. 12

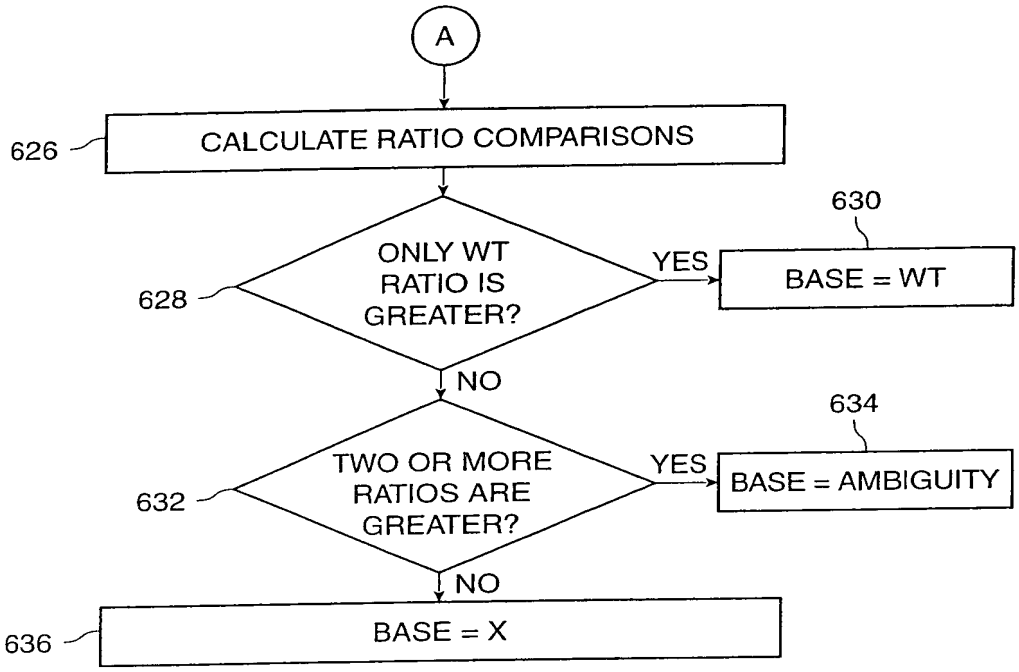


FIG. 12
(CONTINUED)

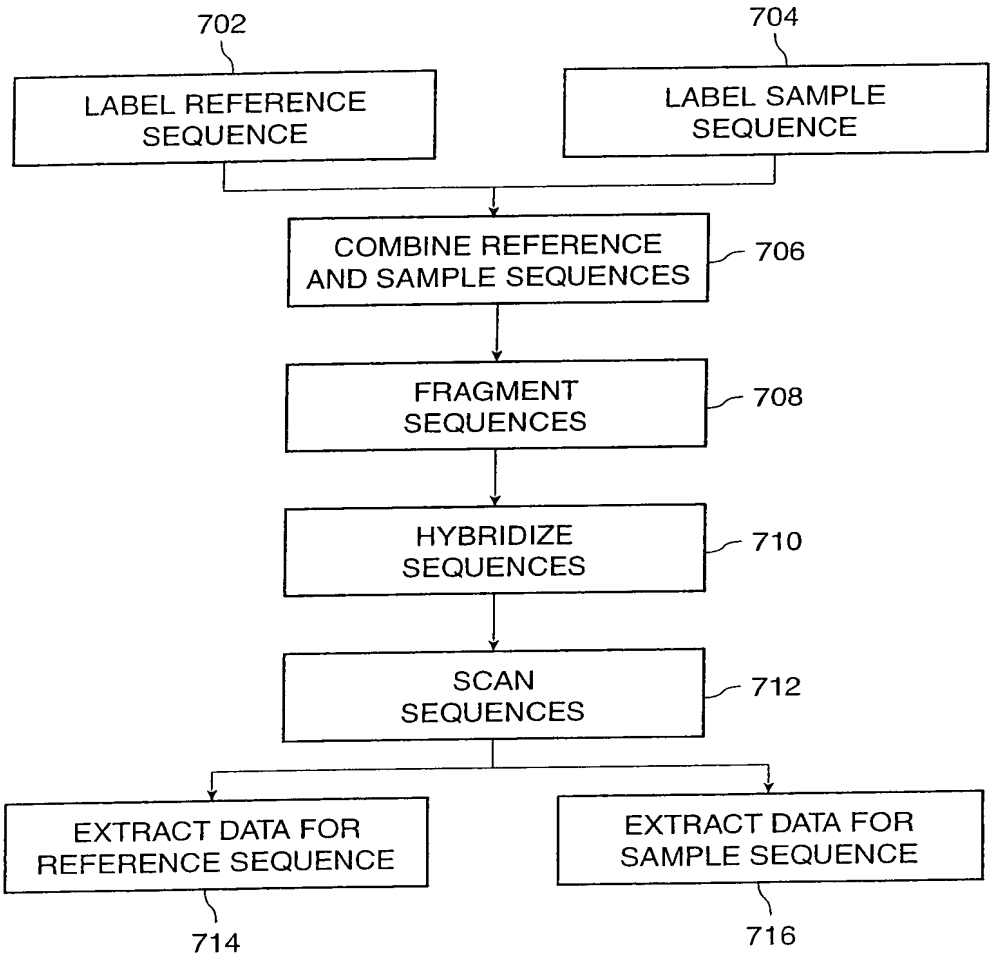

702
LABEL REFERENCE SEQUENCE
704
LABEL SAMPLE SEQUENCE
COMBINE REFERENCE AND SAMPLE SEQUENCES
706
FRAGMENT SEQUENCES
708
HYBRIDIZE SEQUENCES
710
SCAN SEQUENCES
712
EXTRACT DATA FOR REFERENCE SEQUENCE
714
EXTRACT DATA FOR SAMPLE SEQUENCE
716

FIG. 13

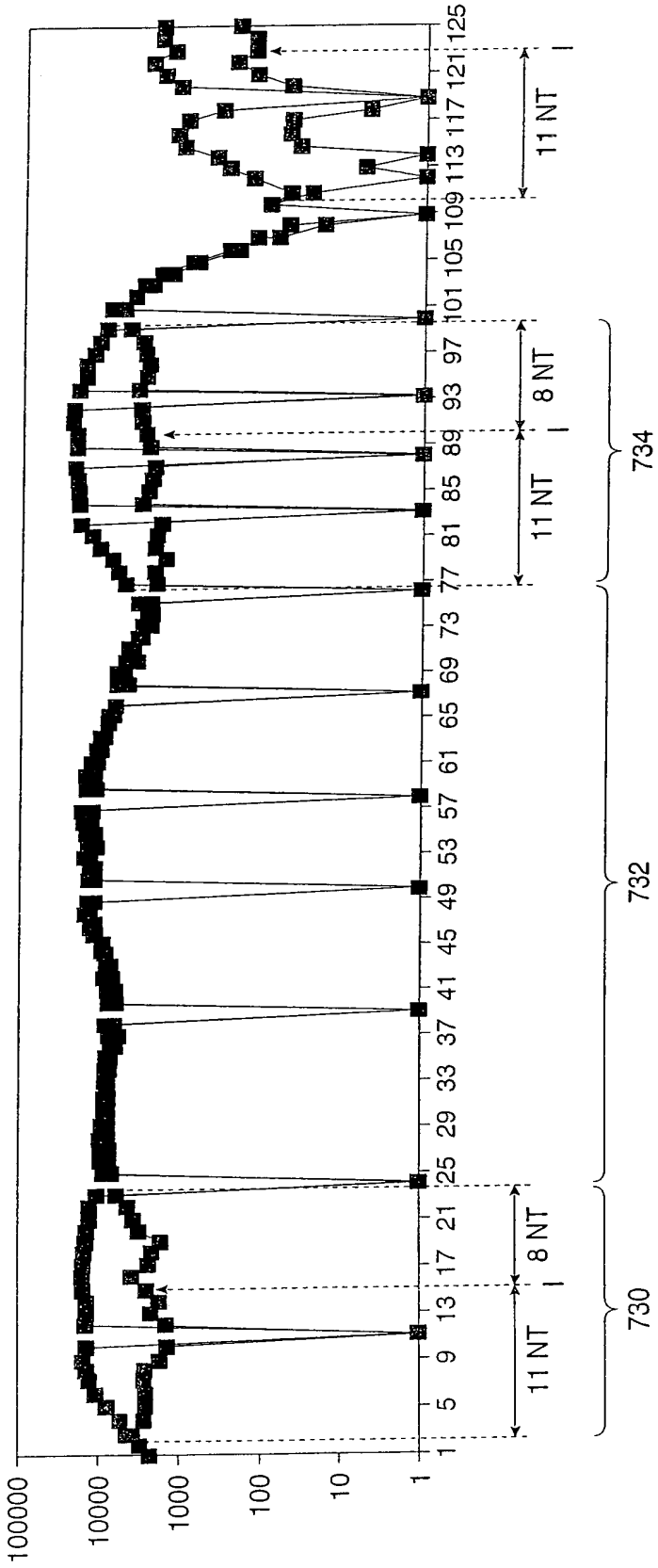

100000
10000
1000
100
10
1
1
5
9
13
17
21
25
29
33
37
41
45
49
53
57
61
65
69
73
77
81
85
89
93
97
101
105
109
113
117
121
125
11 NT
8 NT
11 NT
8 NT
11 NT
730
732
734

FIG. 14A

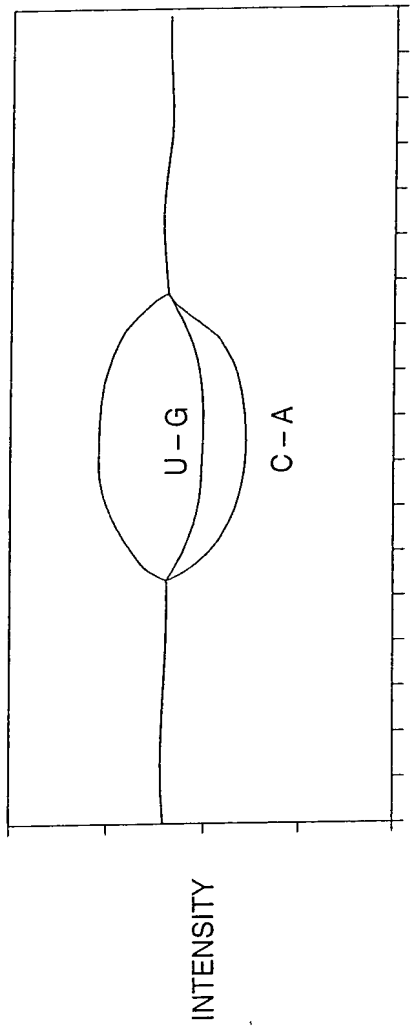


FIG. 14B

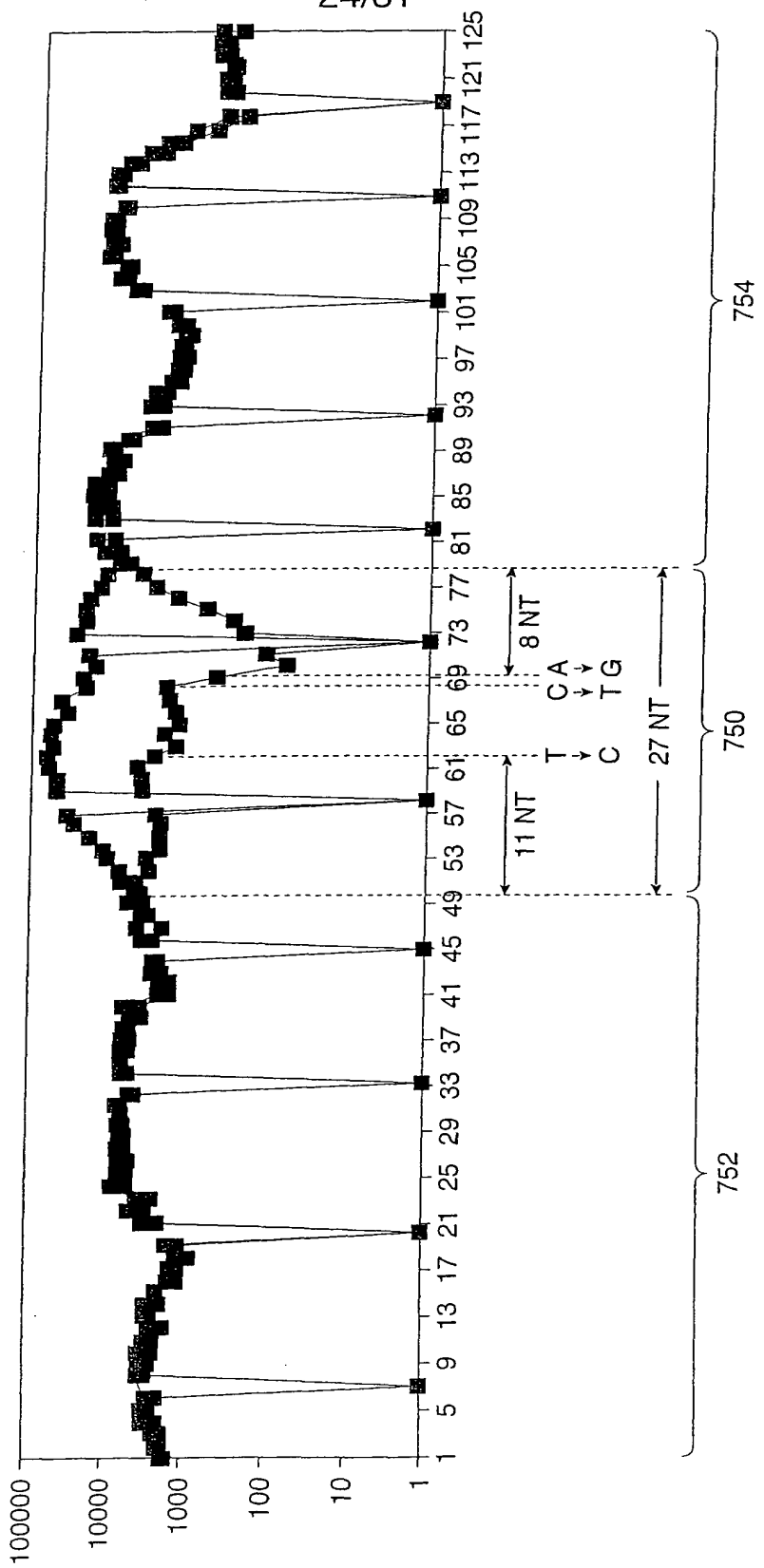

100000
10000
1000
100
10
1
1 5 9 13 17 21 25 29 33 37 41 45 49 53 57 61 65 69 73 77 81 85 89 93 97 101 105 109 113 117 121 125
11 NT
T → C
C A → T G
8 NT
27 NT
752
750
754

FIG. 14C

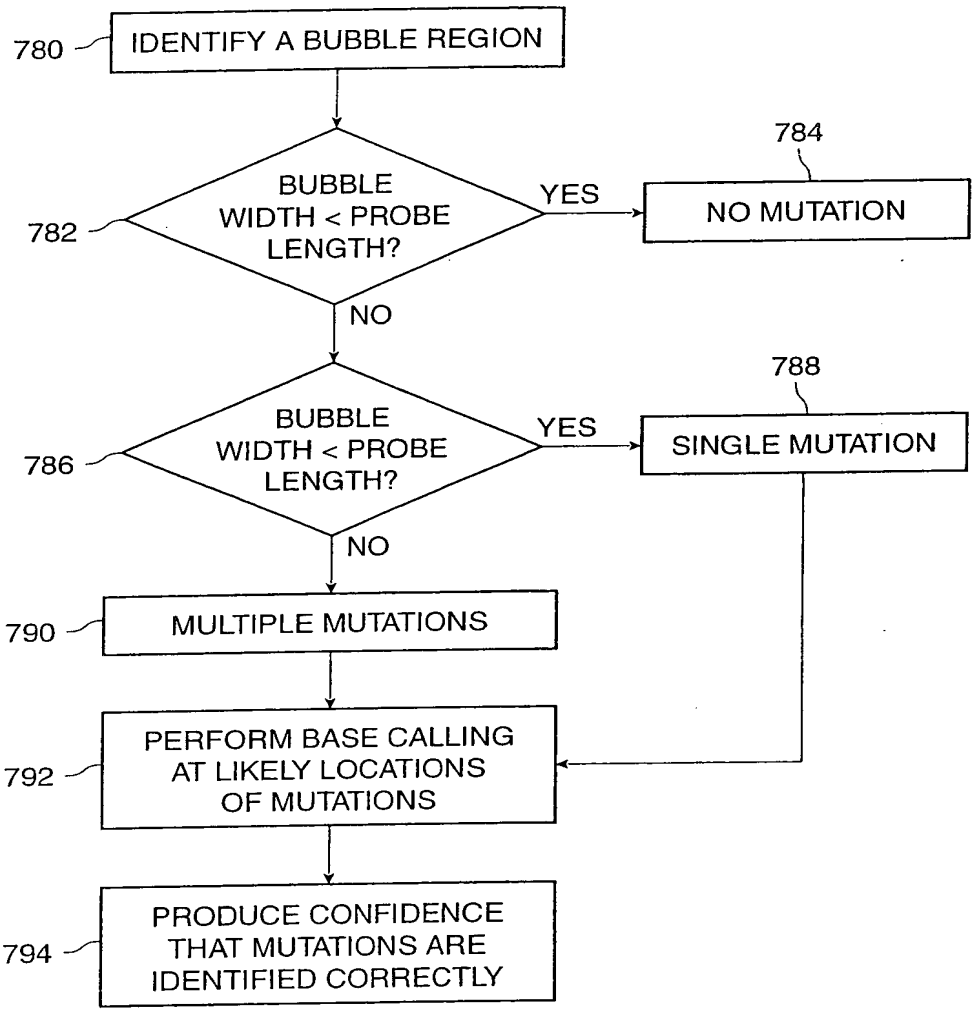
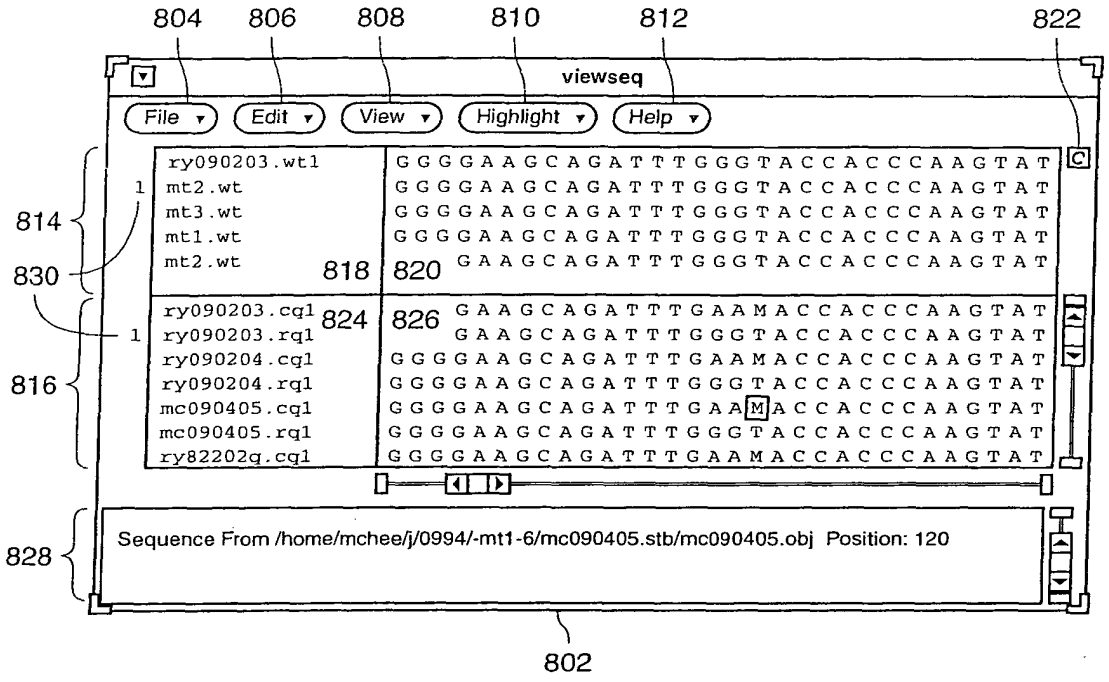

780
IDENTIFY A BUBBLE REGION
782
BUBBLE WIDTH < PROBE LENGTH?
YES
784
NO MUTATION
NO
786
BUBBLE WIDTH < PROBE LENGTH?
YES
788
SINGLE MUTATION
NO
790
MULTIPLE MUTATIONS
792
PERFORM BASE CALLING AT LIKELY LOCATIONS OF MUTATIONS
794
PRODUCE CONFIDENCE THAT MUTATIONS ARE IDENTIFIED CORRECTLY

FIG. 15


804
806
808
810
812
822
viewseq
File
Edit
View
Highlight
Help
ry090203.wt1
mt2.wt
mt3.wt
mt1.wt
mt2.wt
818
820
814
830
ry090203.cq1
ry090203.rq1
ry090204.cq1
ry090204.rq1
mc090405.cq1
mc090405.rq1
ry82202q.cq1
824
826
816
828
Sequence From /home/mchee/j/0994/-mt1-6/mc090405.stb/mc090405.obj Position: 120
802

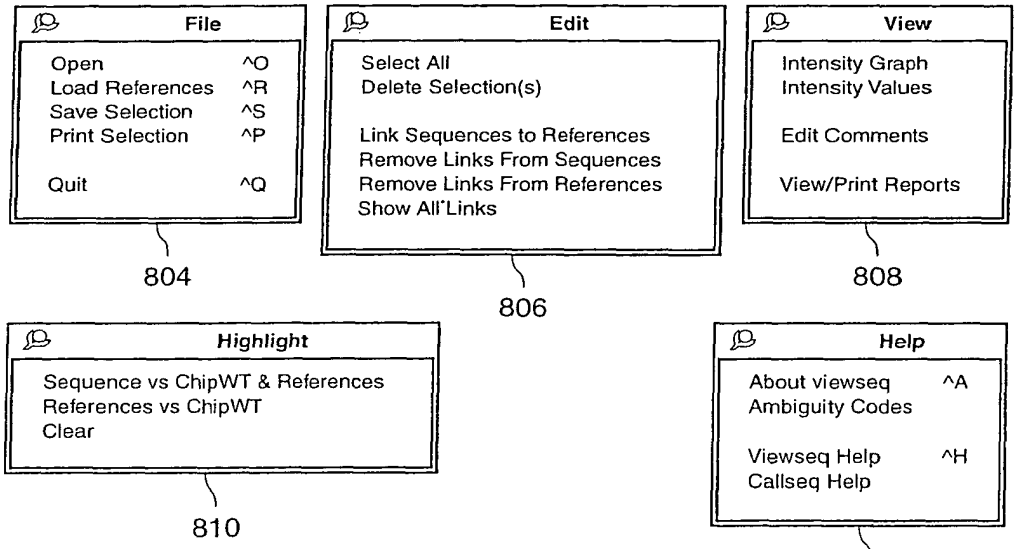

File
Open ^O
Load References ^R
Save Selection ^S
Print Selection ^P
Quit ^Q
804
Edit
Select All
Delete Selection(s)
Link Sequences to References
Remove Links From Sequences
Remove Links From References
Show All Links
806
View
Intensity Graph
Intensity Values
Edit Comments
View/Print Reports
808
Highlight
Sequence vs ChipWT & References
References vs ChipWT
Clear
810
Help
About viewseq ^A
Ambiguity Codes
Viewseq Help ^H
Callseq Help
812

FIG. 16

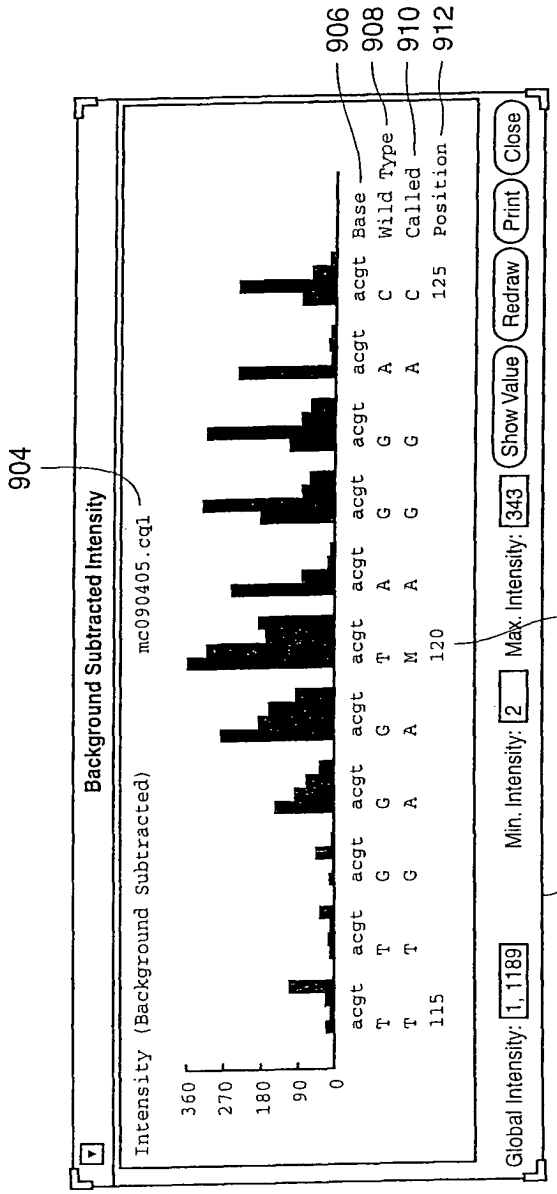

Background Subtracted Intensity
Intensity (Background Subtracted)
mc090405.cq1
360
270
180
90
0
acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt Base
T T G G G T A G G A C Wild Type
T T G A A M A G G A C Called
115 120 125 Position
Global Intensity: 1, 1189
Min. Intensity: 2
Max. Intensity: 343
Show Value
Redraw
Print
Close
904
906
908
910
912
914
902

FIG. 17

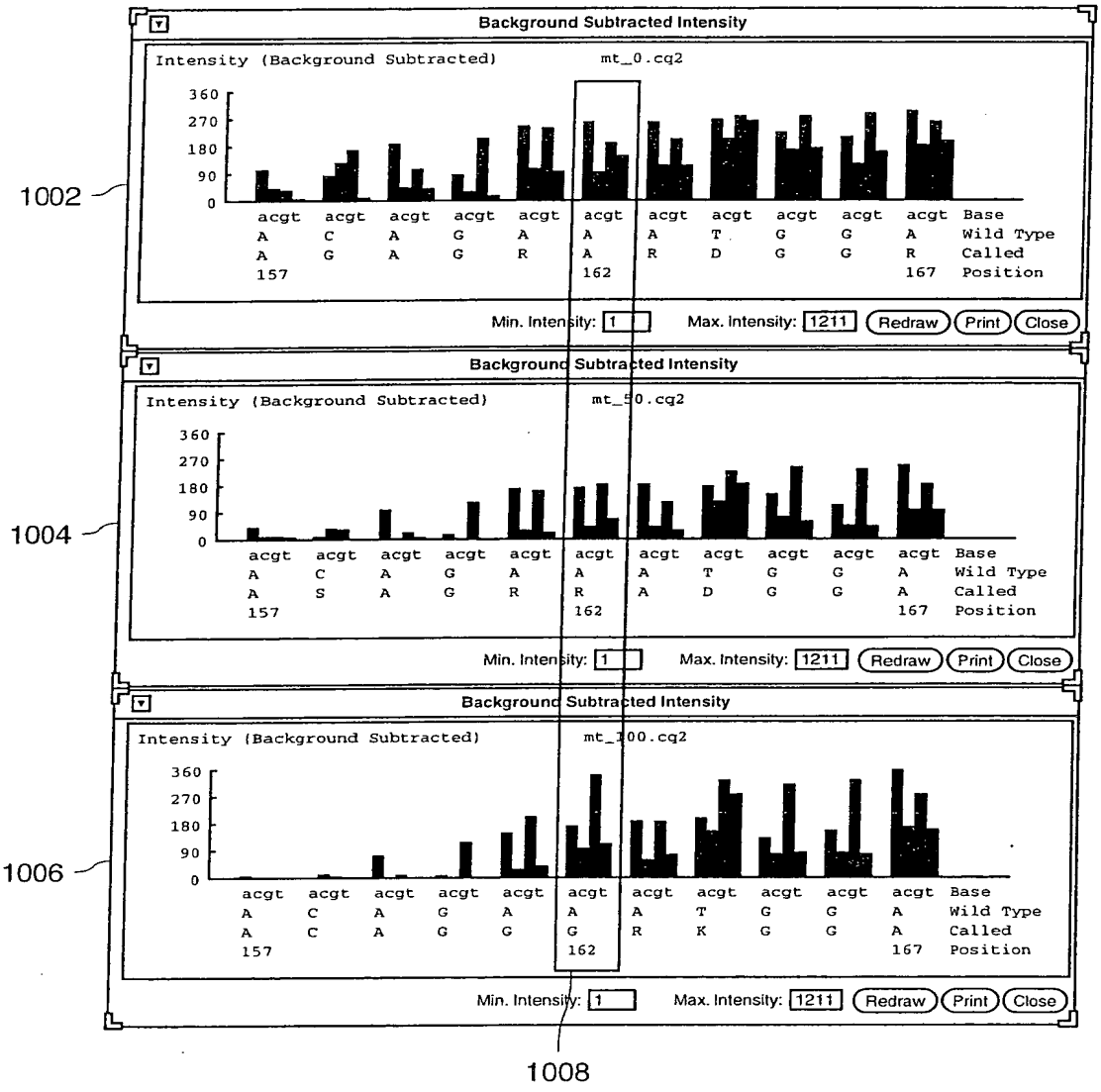

Background Subtracted Intensity
Intensity (Background Subtracted)
mt_0.cq2
360
270
180
90
0
acgt A A 157
acgt C G
acgt A A
acgt G G
acgt A R
acgt A A 162
acgt A R
acgt T D
acgt G G
acgt G G
acgt A R 167
Base Wild Type Called Position
Min. Intensity: 1
Max. Intensity: 1211
Redraw
Print
Close
Background Subtracted Intensity
Intensity (Background Subtracted)
mt_50.cq2
360
270
180
90
0
acgt A A 157
acgt C S
acgt A A
acgt G G
acgt A R
acgt A R 162
acgt A A
acgt T D
acgt G G
acgt G G
acgt A A 167
Base Wild Type Called Position
Min. Intensity: 1
Max. Intensity: 1211
Redraw
Print
Close
Background Subtracted Intensity
Intensity (Background Subtracted)
mt_100.cq2
360
270
180
90
0
acgt A A 157
acgt C C
acgt A A
acgt G G
acgt A G
acgt A G 162
acgt A R
acgt T K
acgt G G
acgt G G
acgt A A 167
Base Wild Type Called Position
Min. Intensity: 1
Max. Intensity: 1211
Redraw
Print
Close
1002
1004
1006
1008

FIG. 18

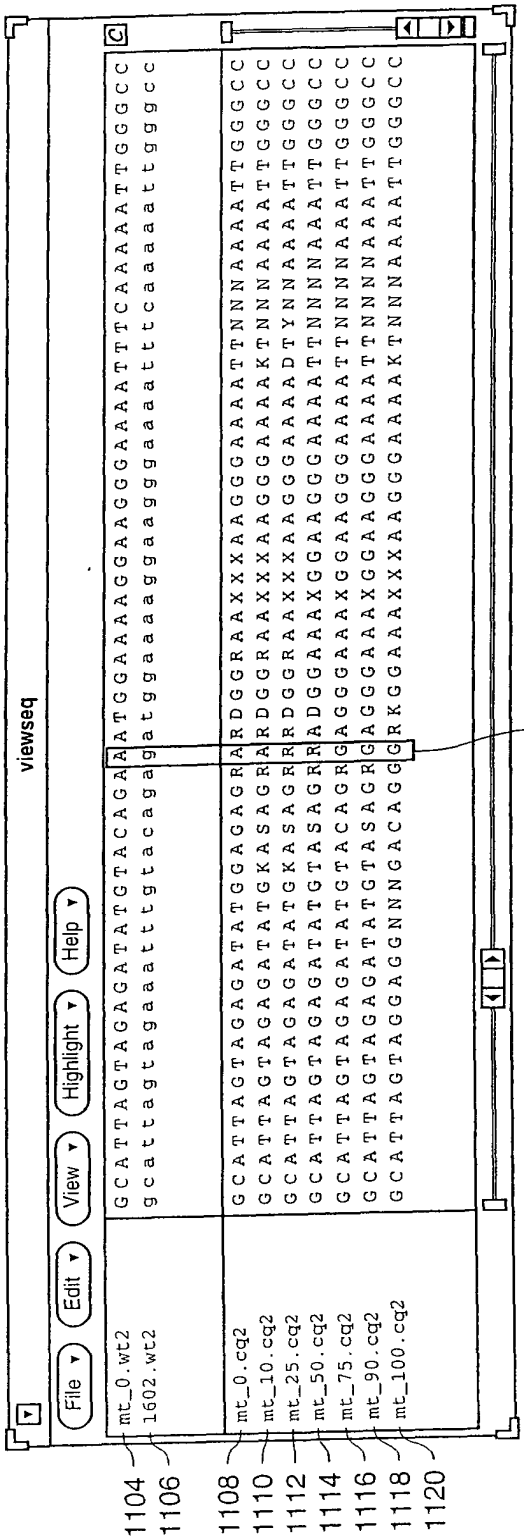

viewseq
File
Edit
View
Highlight
Help
mt_0.wt2
1602.wt2
mt_0.cq2
mt_10.cq2
mt_25.cq2
mt_50.cq2
mt_75.cq2
mt_90.cq2
mt_100.cq2
1104
1106
1108
1110
1112
1114
1116
1118
1120
1108

FIG. 19

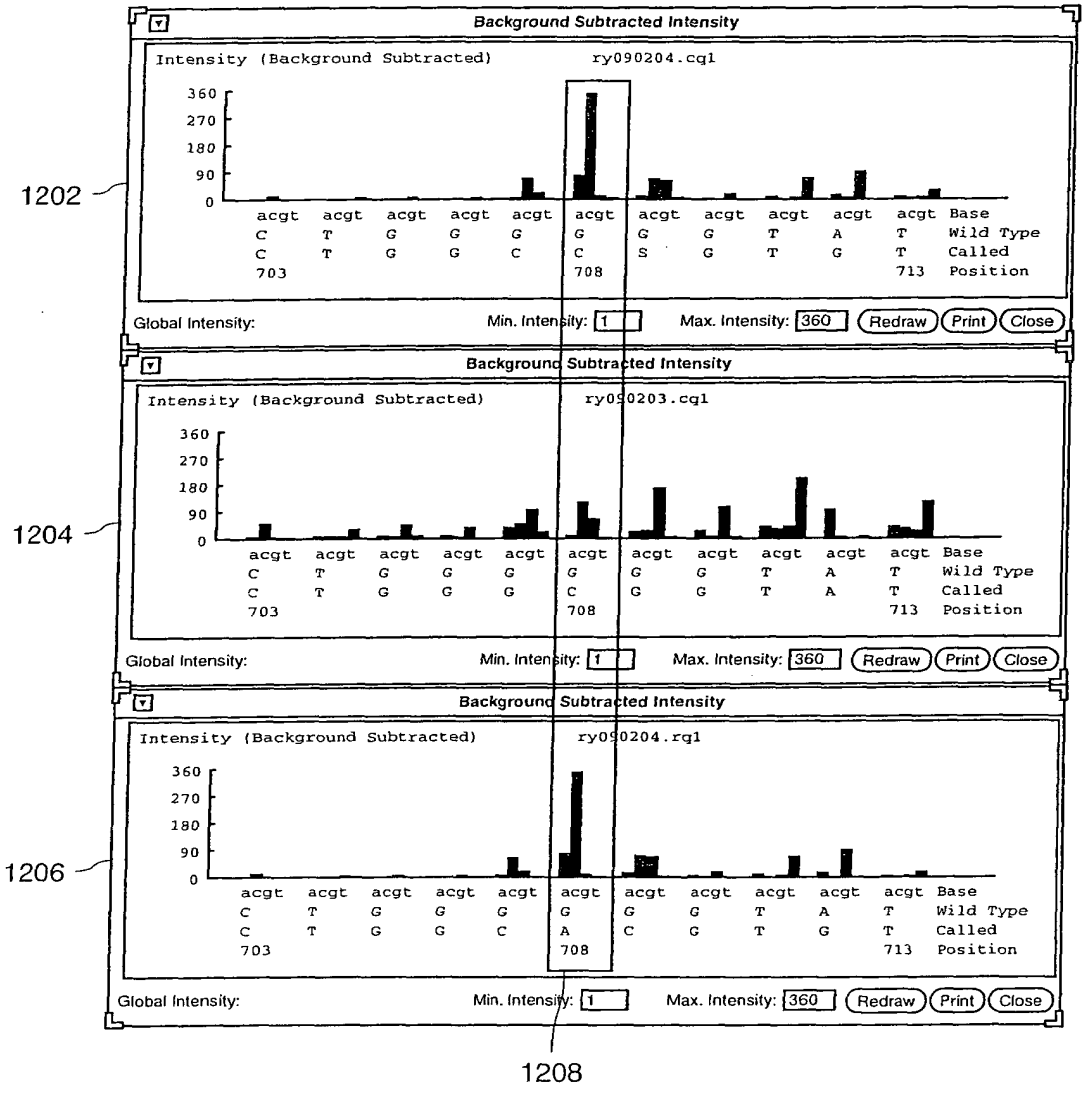

Background Subtracted Intensity
Intensity (Background Subtracted)
ry090204.cql
360
270
180
90
0
acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt Base
C T G G G G G G T A T Wild Type
C T G G C C S G T G T Called
703 708 713 Position
Global Intensity:
Min. Intensity: 1
Max. Intensity: 360
Redraw
Print
Close
Background Subtracted Intensity
Intensity (Background Subtracted)
ry090203.cql
360
270
180
90
0
acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt Base
C T G G G G G G T A T Wild Type
C T G G G C G G T A T Called
703 708 713 Position
Global Intensity:
Min. Intensity: 1
Max. Intensity: 360
Redraw
Print
Close
Background Subtracted Intensity
Intensity (Background Subtracted)
ry090204.rgl
360
270
180
90
0
acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt acgt Base
C T G G G G G G T A T Wild Type
C T G G C A C G T G T Called
703 708 713 Position
Global Intensity:
Min. Intensity: 1
Max. Intensity: 360
Redraw
Print
Close
1202
1204
1206
1208

FIG. 20


tcgagataatctatgtcctcgtctactatgtcataatcttctttacttaaacggtccttttacctttggtttttactatc CONSENSUS
90 100 110 120 130 140 150 160
nngagatannntatgtcctcgtcyactatgtnannnnnnnnnnnnnnnaaacggtcctnnnnnnnnnnnnnnnnnnnnwn
tcgagataatctatgtcctcgtctactatgtcataatnnnnnnnnacttaaacggtcctttttacctttggtttttactatc
tcgagataatctatgtcctcgtctactatgtcataatcttctttacttaaacggtccttttacctttggtttttactatc PRE-TREATMENT
tcgagataatctatgtcctcgtctactatgtcataatcttctttacttaaacggtccttttacctttggtttttactatc
ncgggatantntatgtcctcgtcyactatgtcannnnnncnnncnnnnncaaacggtcchccnnnnnncnnnnnnncnncyaha
tcgrgataatctatgtcctcgtctactatgtcataatccnnncnnctcaaacggtcctyccnnnnytggttnytactatc POST-TREATMENT
tcgagataatctatgtcctcgtctactatgtcataatcchnnctactcaaacggtccttctacctttggtttttactatc
tcgagataatctatgtcctcgtctactatgtcataatcttctttacycaaacggtcctxctacctttggtttttactatc
ccccttaacctccaaaatagtttcattctgtcatgctagtctatggacatctttagacacctgtatttcgatatccatgt CONSENSUS
170 180 190 200 210 220 230 240
cnncntaacctccaaaatannnnnnnntctnnnnnnannnntctannngnagnnnnaganarnccnnnnnnnnnnatncatgt
cccccttaacctccaaaatagtttcattctgncatannagtctatgngnngnnntagacagncnnnnntcgatatccatgt
cmmcttaacctccaaaatagtttcattctgtcatactagtctatgggtagctttagacamccgtatttcgatatccatgt PRE-TREATMENT
ccmcttaacctccaaaatagtttcattctgtcatactagtctatgggtagctttagacacccgtatttcgatatccatgt
aawcycaacctccaaaatannnnnnnntctnnnnnnannncnctnnnnnnnagngnnagacacctgtatnnnnntatncaygt
cccccttaacctccaaaatagtttcattctgncatacnnstctannxnnagxgttagacacctgtatttcgatatccatgt POST-TREATMENT
cmccttaacctccaaaatagtttcattctgtcatactagtctatgagtagctttagacacctgtatttcgatatccatgt
ccmcttaacctccaaaatagtttcattctgtcatactagtctatgagtagctttagacacctgtatttcgatatccatgt

FIG. 21